

FIG. 2

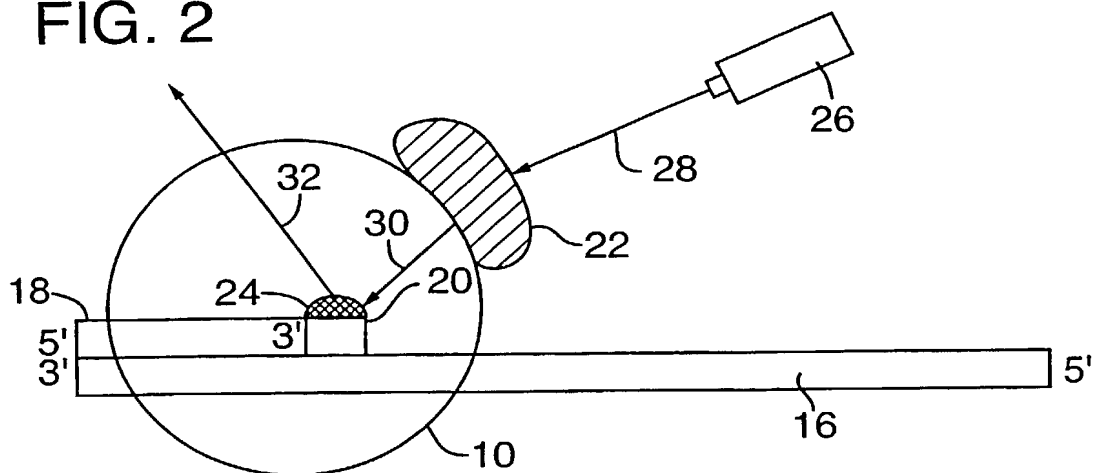
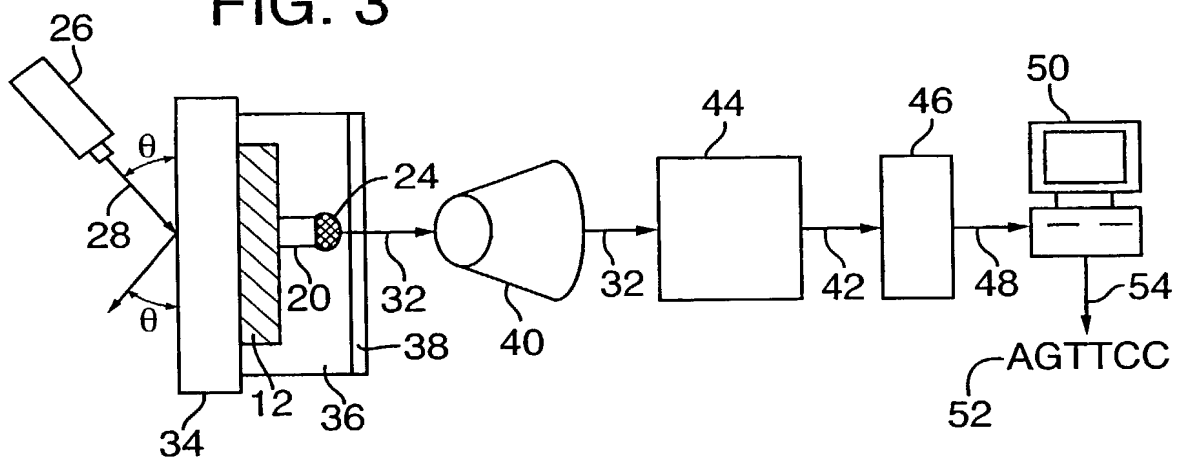
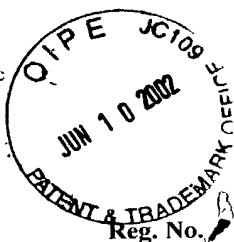


FIG. 3





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E-033-99/1 PATENT

Atty. Ref. No. 4239-62263

2002 052

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The Assignee certifies that the above-identified Assignment has been reviewed and to the best of Assignee's knowledge and belief, title is in the Assignee, as demonstrated by the copy of the Assignment submitted herewith.

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The National Institutes of Health Office of Technology Transfer has been duly delegated responsibility for patent matters under the authority of the memorandum dated May 21, 1991, from Louis W. Sullivan, the Secretary of the Department of Health and Human Services, delegating the authority to the Heads of the Public Health Service Operating Divisions, as well as a memorandum dated October 9, 2001, from Mark L. Rohrbach, Ph.D., J.D., Acting Director, Office of Technology Transfer, National Institutes of Health, delegating authority to sign this Power of Attorney to the undersigned individual. The undersigned is therefore authorized to exercise such authority in this matter.

Executed on May 24, 2002, at Rockville, Maryland.

UNITED STATES DEPARTMENT OF  
HEALTH AND HUMAN SERVICES

Richard U. Rodriguez  
 Name: Richard U. Rodriguez  
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SLR.dm 04/18/02 111928.doc

E-033-99/1 PATENT  
Atty. Ref. No. 4239-62263

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Schneider et al.

Art Unit: Not yet assigned

Application No. 10/070,053

CERTIFICATE OF MAILING

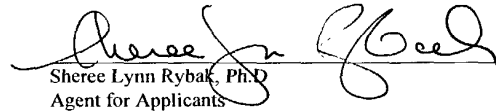
Filed: February 28, 2002

For: HIGH SPEED PARALLEL MOLECULAR  
NUCLEIC ACID SEQUENCING

Examiner: Not yet assigned

Date: April 18, 2002

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service on 6-3-02 as First Class Mail in an envelope addressed to:  
COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231.

  
Sheree Lynn Rybak, Ph.D.  
Agent for Applicants

**REVOCATION OF PRIOR POWER OF ATTORNEY, NEW POWER OF ATTORNEY  
BY ASSIGNEE AND CERTIFICATE BY ASSIGNEE UNDER 37 CFR § 3.73**

COMMISSIONER FOR PATENTS  
WASHINGTON D.C. 20231

THE GOVERNMENT OF THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES is the Assignee of the entire right, title and interest in the above-identified patent application, as evidenced by the Assignment

- ☒ attached hereto.  
☐ recorded in the U.S. Patent and Trademark Office at Reel , Frame(s)

The Assignee hereby revokes all prior powers of attorney for this matter, and appoints as its representatives to conduct all business in the Patent and Trademark Office connected therewith the attorneys and agents identified below:

Name	Reg. No.	Name	Reg. No.
James C. Haight	<u>25,588</u>	Jack Spiegel	<u>34,477</u>
Robert Benson	<u>33,612</u>	David R. Sadowski	<u>32,808</u>
Susan S. Rucker	<u>35,762</u>	Steve Ferguson	<u>38,448</u>
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Stephen L. Finley	<u>36,357</u>	Marlene Shinn	<u>46,005</u>
Norbert Pontzer	<u>40,777</u>		

all of the National Institutes of Health, Office of Technology Transfer, 6011 Executive, Boulevard, Suite #325, Rockville, MD 20852; and grants an Associate Power of Attorney to the attorneys and agents listed below:

**ASSIGNMENT**

WHEREAS, we, Thomas D. Schneider, of 107 Alessandra Ct. #208, Frederick, MD 21702-4015, a citizen of the United States of America, and Denise Rubens, of 13815 Motters Station Road, Rocky Ridge, MD 21778, a citizen of the United States of America, employees of the Department of Health and Human Services at the time the invention was made, have invented HIGH SPEED PARALLEL MOLECULAR NUCLEIC ACID SEQUENCING for which a provisional patent application has been sent to the Assistant Commissioner for Patents and is identified as U.S. Provisional Patent Application Serial No. 60/151,580 filed August 30, 1999.

WHEREAS, we by virtue of this assignment, and the conditions under which said invention was made are such as to entitle the Government of the United States of America under Paragraph 1(a) of Executive order 10096, to the entire right, title, and interest herein, both domestic and foreign; and

WHEREAS, the Government of the United States of America is desirous of acquiring all domestic and foreign right, title, and interest in the aforesaid invention described in the aforesaid application for Letters Patent of the United States of America; and

NOW, THEREFORE, to all whom it may concern, be it known for and in consideration of the premises and other valuable considerations, we the undersigned, have sold, assigned, and transferred and by these presents do sell, assign, and transfer unto The Government of the United States of America as represented by the Secretary of the Department of Health and Human Services (hereinafter THE GOVERNMENT), and his successors, the full and exclusive right, title, and interest throughout the United States of America, its territories and dependencies, and within each and every foreign country in which THE GOVERNMENT elects to file patent applications on the invention described in the aforesaid application, and all Letters Patents and Registrations which may be granted for corresponding non-provisional patent applications on the same in the United States of America and all countries throughout the world, and to claim the priority from the application as provided by United States law and the Paris Convention, or of any divisional, renewal, continuation in whole or in part, substitution, conversion, reissue, prolongation or extension thereof.

AND, we hereby authorize and request the Assistant Commissioner for Patents to issue said Letters Patent to THE GOVERNMENT as an assignee of the entire right, title, and interest in and to the same throughout the United States of America, its territories and dependencies, and within each and every foreign country in which THE GOVERNMENT elects to file, for the sole use for the full term or terms for which said Letters Patent and Registrations may be granted thereon, or of any division, renewal, continuation in whole or in part, substitution, conversion, reissue, prolongation or extension thereof which may be granted as fully and entirely as the same would have been held by us, had this assignment not been made;

AND, we hereby warrant that there are no outstanding assignments, grants, liens, encumbrances, or agreements either written, oral, or implied with respect to the aforesaid application for Letters Patent which will impair, diminish, limit, or abridge the interest herein conveyed at the time of the execution of this instrument by us;

AND, we hereby agree to execute any and all applications for Letters Patent in the United States of America and foreign countries, and to furnish and deliver to the Secretary, Department of Health and Human Services, upon request, all data and documents, and to execute any papers which may be necessary for the prosecution of any application or applications of Letters Patent or for THE GOVERNMENT to exercise its rights granted hereunder, including communicating to THE GOVERNMENT, its representatives or agents, any facts relating to said invention, including evidence for interference purposes, or for other proceedings, whenever requested, to testify in any interference or other proceedings, whenever requested, and to execute and deliver on request all lawful papers required to make any of the foregoing provisions effective, and likewise make these provisions binding upon our heirs, legal representatives, administrators and assigns, and we shall assist THE GOVERNMENT in every way as may be requested in protecting said invention, provided

that any expense of extending such assistance shall be paid by THE GOVERNMENT.

The undersigned hereby grants the law firm of Klarquist Sparkman Campbell Leigh & Whinston, LLP, the power to insert on this Assignment any further identification which may be necessary or desirable in order to comply with the rules of the United States Patent and Trademark Office for recordation of this document.

IN TESTIMONY WHEREOF, Assignors have signed their names on the dates indicated.

Dated: Jan 24, 2000

*rw* Thomas D. Schneider  
Thomas D. Schneider

STATE OF Maryland )  
Frederick ) ss.  
COUNTY OF ~~Montgomery~~ )

This 24 day of January, 2000, \_\_\_\_\_, before me personally came the above-named Thomas D. Schneider, who executed the foregoing Assignment in my presence, and who acknowledged to me that he executed the same of his own free will for the purposes set forth therein.

*o* Kathy Louise Easterday  
Kathy Louise Easterday  
Notary Public for Maryland  
My commission expires: 8/01/03

[SEAL]

Dated: Jan 24, 2000

*2w* Denise Rubens  
Denise Rubens

STATE OF Maryland )  
Frederick ) ss.  
COUNTY OF ~~Montgomery~~ )

This 24 day of January, 2000, \_\_\_\_\_, before me personally came the above-named Denise Rubens, who executed the foregoing Assignment in my presence, and who acknowledged to me that he executed the same of his own free will for the purposes set forth therein.

Kathy Louise Easterday  
Kathy Louise Easterday  
Notary Public for Maryland  
My commission expires: 8/01/03

[SEAL]

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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(10) International Publication Number  
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- (51) International Patent Classification<sup>7</sup>: **C12Q 1/68, G01N 21/64**
- (21) International Application Number: **PCT/US00/23736**
- (22) International Filing Date: **29 August 2000 (29.08.2000)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data:  
**60/151,580 30 August 1999 (30.08.1999) US**
- (71) Applicant (for all designated States except US): **THE GOVERNMENT OF THE UNITED STATES OF AMERICA, as represented by THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES [US/US]; The National Institutes of Health, Office of Technology Transfer, Suite #325, 6011 Executive Boulevard, Rockville, MD 20852 (US).**
- (72) Inventors; and  
(75) Inventors/Applicants (for US only): **SCHNEIDER, Thomas, D. [US/US]; 107 Alessandra Court, #208, Frederick, MD 21702-4015 (US); RUBENS, Denise [US/US]; 13815 Motters Station Road, Rocky Ridge, MD 21778 (US).**
- (74) Agent: **NOONAN, William, D.; Klarquist, Sparkman, Campbell, Leigh & Whinston, LLP, Suite 1600, One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).**
- (81) Designated States (national): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.**
- (84) Designated States (regional): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).**
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- (88) Date of publication of the international search report:  
**4 October 2001**
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **HIGH SPEED PARALLEL MOLECULAR NUCLEIC ACID SEQUENCING**

(57) Abstract: A method and device is disclosed for high speed, automated sequencing of nucleic acid molecules. A nucleic acid molecule to be sequenced is exposed to a polymerase in the presence of nucleotides which are to be incorporated into a complementary nucleic acid strand. The polymerase carries a donor fluorophore, and each type of nucleotide (e.g. A, T/U, C and G) carries a distinguishable acceptor fluorophore characteristic of the particular type of nucleotide. As the polymerase incorporates individual nucleic acid molecules into a complementary strand, a laser continuously irradiates the donor fluorophore, at a wavelength that causes it to emit an emission signal (but the laser wavelength does not stimulate the acceptor fluorophore). In particular embodiments, no laser is needed if the donor fluorophore is a luminescent molecule or is stimulated by one. The emission signal from the polymerase is capable of stimulating any of the donor fluorophores (but not acceptor fluorophores), so that as a nucleotide is added by the polymerase, the acceptor fluorophore emits a signal associated with the type of nucleotide added to the complementary strand. The series of emission signals from the acceptor fluorophores is detected, and correlated with a sequence of nucleotides that correspond to the sequence of emission signals.

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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number  
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(51) International Patent Classification<sup>7</sup>: C12Q 1/68,  
G01N 21/64

(21) International Application Number: PCT/US00/23736

(22) International Filing Date: 29 August 2000 (29.08.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/151,580 30 August 1999 (30.08.1999) US

(71) Applicant (for all designated States except US): **THE GOVERNMENT OF THE UNITED STATES OF AMERICA**, as represented by **THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES** [US/US]; The National Institutes of Health, Office of Technology Transfer, Suite #325, 6011 Executive Boulevard, Rockville, MD 20852 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **SCHNEIDER, Thomas, D.** [US/US]; 107 Alessandra Court, #208, Frederick, MD 21702-4015 (US). **RUBENS, Denise** [US/US]; 13815 Motters Station Road, Rocky Ridge, MD 21778 (US).

(74) Agent: **NOONAN, William, D.**; Klarquist, Sparkman, Campbell, Leigh & Winston, LLP, Suite 1600, One World Trade Center, 121 SW Salmon Street, Portland, OR 97204 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

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4 October 2001

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